U30066PCT
Charité - Universitätsmedizin Berlin

Claims:

1. Use of at least one proteasome inhibitor for the treatment of fibrotic diseases, which are not caused by inflammatory responses to foreign matters.

2. Use according to claim 1 for the treatment of a cardiac fibrosis caused by overload, a liver fibrosis caused by congestion, a kidney fibrosis caused by high pressure or a joint fibrosis in case of a joint malposition.

3. Use according to claim 2 for the treatment of a cardiac fibrosis caused by overload under chronic pressure stress in arterial hypertension and/or for the treatment of a cardiac fibrosis caused by overload in compensatory hyperkinesia of the intact residual myocardium in case of myocardial infarction.

4. Use according to claim 2 or 3 for the treatment of a cardiac fibrosis, in which a treatment with ACE inhibitors, AT-1-antagonists and/or endothelin receptor antagonists is indicated.

5. Use according to one or several of the claims 1 to 4, wherein a patient is administered at least one proteasome inhibitor in a dose of approximately 0,5 µg/kg body weight to approximately 0,5 mg/kg body weight, preferably in a dose of approximately 1 µg/kg body weight to approximately 0,1 mg/kg body weight, preferably in a dose of approximately 0,01 mg/kg body weight to approximately 0,1 mg/kg body weight.

6. Use according to one or several of the claims 1 to 5, characterised in that the fibrotic diseases relate to fibrotic organ diseases, preferably of the lung, liver, skin, joints, skeleton and/or glands, in particular to diseases of the cardiovascular system.

7. Use according to one or several of the claims 1 to 6, characterised in that the proteasome inhibitor is a low-molecular organic compound or a molecular-biological compound.

8. Use according to claim 7, characterised in that the proteasome inhibitor is a threonine protease inhibitor, a serine protease inhibitor, a cysteine protease inhibitor, a gene expression inhibitor of the proteasomal system and/or a binding protein or binding peptide directed against at least one component of the proteasomal system, preferably against ubiquitin and/or against the proteasome.

9. Use according to claim 7 or 8, characterised in that the proteasome inhibitor is a peptide aldehyde, a peptide boronate, a peptide vinyl sulfone, a peptide epoxyketone, a lactacystine, a peptide alpha keto-aldehyde, an alpha-ketoamide, an indanone peptide, a polyalkylene aldehyde, a polyphenol, in particular a cathechin-3-gallate, a nucleic acid directed against at least one component of the proteasomal system and/or an antibody or binding-reactive part or derivative thereof, directed against at least one component of the proteasomal system.

10. Use according to one of the claims 7-9, characterised in that the proteasome inhibitor is Z-Leu-Leu-Leu-al (MG132), Z-Ile-Glu(OtBu)-Ala-Leu-al (PSI), CEP1612, pyrazylcarbonyl-Phe-Leu-boronate (PS-341), dansyl-Phe-Leu-boronate (DFLB), morpholino-naphthylalanine-Leu-boronate (MG273), NIP-Leu_3-vinylsulfone (NLVS), Tyr-Leu_3-VS, NIP-Leu-Leu-Asn-VS, Ada-Tyr-Ahx_3-Leu_3-VS, Ada-Lys(Bio)-Ahx_3-Leu_3-VS, Ac(Me)-Ile-Ile-Thr-Leu-EX (epoxomicin), dihydroeponemycin, lactacystine, clasto-lactacystine-beta-lactone (omuralide), PS-519, Ac-Leu-Leu-Nle-al (ALLN), 3,4-dichloroisocoumarine (DCI), 4-(2-aminoethyl)-benzenesulfonyl fluoride (Pefablock SC), TMC-95A, gliotoxin, (-)-epigallocatechin-3-gallate (EGCG), ritonavir, lovastatin, aclacinomicin A (Aclarubicin), cyclosporin, an anti-sense-RNA or a double-stranded RNA (dsRNA) against a proteasome encoding sequence, a triplex forming oligonucleotide against a proteasome encoding sequence and/or a knock-out construct against a proteasome encoding sequence, wherein Z is a benzyloxycarbonyl group, al is an aldehyde group, VS is a vinyl sulfone group, NIP is a 3-nitro-4-hydroxy-5-iodophenylacetate group, and Bio is a biotin group.